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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/612,179	07/02/2003	Roland Kreutzer	20200/2093D	5239
29933	7590	03/10/2005	EXAMINER	
PALMER & DODGE, LLP KATHLEEN M. WILLIAMS 111 HUNTINGTON AVENUE BOSTON, MA 02199			VIVLEMORE, TRACY ANN	
		ART UNIT		PAPER NUMBER
				1635

DATE MAILED: 03/10/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	Application No.	Applicant(s)
	10/612,179	KREUTZER ET AL.
	Examiner	Art Unit
	Tracy Vivlemore	1635

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 18 January 2005.

2a) This action is FINAL.                            2b) This action is non-final.

3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 4-15 is/are pending in the application.

4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.

5) Claim(s) \_\_\_\_\_ is/are allowed.

6) Claim(s) 4-15 is/are rejected.

7) Claim(s) \_\_\_\_\_ is/are objected to.

8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.

10) The drawing(s) filed on 02 July 2003 is/are: a) accepted or b) objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) All    b) Some \* c) None of:

- Certified copies of the priority documents have been received.
- Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
- Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

1) Notice of References Cited (PTO-892)

2) Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date see box 6.

4) Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_

5) Notice of Informal Patent Application (PTO-152)

6) Other: 1/12/04, 1/16/04, 5/18/04

## **DETAILED ACTION**

### ***Information Disclosure Statement***

The information disclosure statements filed January 12 and 16, 2004 fail to comply with 37 CFR 1.98(a)(3) because they do not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of each patent listed that is not in the English language. The German language patents that have no translation have been placed in the application file, but the information referred to therein has not been considered. Additionally, no copy of references identified as DE 102 35 620.3 and DE 199 03 713 could be found in the file and these references have also not been considered.

### ***Specification***

The disclosure is objected to because of the following informalities: the specification may not refer to claims. See for example pages 1 and 2. It is suggested that the content of any claims referred to in the specification be incorporated into the specification.

In addition, the disclosure is objected to because of the following informalities: The heading of each section is missing.

The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

### **Arrangement of the Specification**

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

- (a) TITLE OF THE INVENTION.
- (b) CROSS-REFERENCE TO RELATED APPLICATIONS.
- (c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
- (d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or  
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
- (e) BACKGROUND OF THE INVENTION.
  - (1) Field of the Invention.
  - (2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
- (f) BRIEF SUMMARY OF THE INVENTION.
- (g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).

- (h) DETAILED DESCRIPTION OF THE INVENTION.
- (i) CLAIM OR CLAIMS (commencing on a separate sheet).
- (j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
- (k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

Appropriate correction is required.

#### ***Claim Rejections - 35 USC § 112***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 4-15 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

1. Claim 4 is directed to an isolated double stranded RNA (dsRNA) no more than 21 nucleotides in length that is formed from two separate strands wherein one of the strands is complementary to less than a full-length RNA transcript of a mammalian gene

that inhibits expression of the target gene. Claims 5-9 limit claim 4 by further defining the length of the dsRNA, the nature of the RNA transcript to which the dsRNA is complementary and the dsRNA and the degree of complementarity of the dsRNA. Claim 10 is directed to dsRNA no more than 21 nucleotides in length wherein a linker connects the two complementary strands. Claims 11-15 recite limitations to claim 10 describing the nature of the linker, the nature of the RNA transcript to which the dsRNA is complementary and the dsRNA and the degree of complementarity of the dsRNA for the RNA transcript.

2. The specification teaches on page 4 that the dsRNA has 10-1000 or preferably 15-49 base pairs. The specification does not contemplate a further limitation of the length of the dsRNA to exclude embodiments wherein the dsRNA is 22-49 base pairs and hence does not provide support for the limitation that the dsRNA is no more than 21 nucleotides in length. The specification discloses a single sequence 21 bases in length that is linked to its complementary sequence via a C18 linker that forms a disulfide bond. On page 19 it is clear that the only contemplated use of this 21mer is as a covalent complex with its complement (see lines 15-19), thus the specification does not provide support for dsRNA 21 bases in length that are two separate strands.

### ***Double Patenting***

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

3. Claims 4-8, 10 and 11 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 221-225, 239, 242 and 249 of copending Application No. 09/889,802. Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application would be fully encompassed by the claims of the '802 application.

4. Claims 4 and 10 are directed to dsRNAs no more than 21 nucleotides that are either two separate complementary strands or are linked by a linker. Claim 221 of the '802 application is directed to dsRNAs no more than 49 bases in length containing a 3' overhang. Claim 242 of the '802 application recites that the dsRNA is 21 nucleotides in length. Claim 224 is directed to a dsRNA no more than 49 bases in length formed from

two strands connected by a linker. Claims 222, 223, 239, 249 and 225 recite limitations identical to those of claims 5, 6, 7, 8 and 11, respectively. The claims of the '802 application fully encompass dsRNAs that are 21 nucleotides or less and thus fully encompass the subject matter of the instant claims.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

***Claim Rejections - 35 USC § 102***

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 4, 5 and 7 are rejected under 35 U.S.C. 102(b) as being anticipated by Kmiec (US 5,731,181 March 24, 1998).

5. Claim 4 is directed to an isolated dsRNA no more than 21 nucleotides in length formed from two separate complementary strands, one of which is complementary to part of an RNA transcript of a mammalian gene. Claim 5 states the length of the dsRNA is 15-21 nucleotides and claim 7 states the dsRNA is modified to be resistant to RNA degradation.

6. Kmiec discloses an oligonucleotide known as a chimeric mutational vector (CMV). At column 4 lines 45-62, Kmiec discloses that the CMV is homologous to a target gene, that a CMV can be two separate strands that can be ribonucleotides and

that it can contain nucleotides having 2'-O-modified sugars that are known to increase the resistance of oligonucleotides to degradation. At column 6, lines 19-21, Kmiec discloses that the length of a CMV made of two strands is 20-100. Section 6.1 discloses how such CMVs can be used to introduce changes in the sequence of any eukaryotic gene. Changing the sequence of a gene can include a mutation that causes premature termination of translation or a mutation that changes a protein from an active to an inactive form. Such changes would result in inhibition of expression of the gene.

7. Thus, Kmiec discloses and anticipates claims 4, 5 and 7.

Claims 10-15 are rejected under 35 U.S.C. 102(b) as being anticipated by Agrawal et al. (WO 94/01550, January 20, 1994).

8. Claim 10 is directed to dsRNA no more than 21 nucleotides in length wherein a linker connects the two complementary strands. Claims 11-15 recite limitations to claim 10 reciting that the linker is polyethylene glycol and describing the nature of the RNA transcript to which the dsRNA is complementary, the nature of the dsRNA and the degree of complementarity of the dsRNA for the RNA transcript.

9. Agrawal et al. disclose self-stabilized oligonucleotides useful for antisense therapeutics that comprise a target hybridizing region and a self-complementary region. On page 9, line 30 through page 10 line 1 Agrawal et al. disclose that the target hybridizing region is complementary to a nucleic acid sequence from a variety of sources and is from 8-50 nucleotides in length. On page 15, line 26 through page 17, line 12 Agrawal et al. disclose that the self-complementary region of the oligonucleotide is fully or partially complementary to the hybridizing region, the hybridizing region and

the self-complementary region can be linked by a polyethylene glycol linker and the oligonucleotides of the invention can be ribonucleotides and can contain modifications such as modified phosphate linkers and 2'-O-modified sugars that are known to increase the resistance of oligonucleotides to degradation.

10. Thus, Agrawal et al. disclose all limitations of and anticipate claims 10-15.

### ***Conclusion***

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Tracy Vivlemore whose telephone number is 571-272-2914. The examiner can normally be reached on Mon-Fri 8:45-5:15.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader can be reached on 571-272-0760. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with; the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service

center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public. For more information about the PAIR system, see <http://pair-direct.uspto.gov>.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Tracy Vivlemore  
Examiner  
Art Unit 1635

TV  
March 1, 2005



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1635